2017-00187 - Differential model reduction by (min,+)
tropical algebra constraint solving
Level of qualifications required : Graduate degree or equivalent
Fonction : PhD Position

About the research centre or Inria department
Located at the heart of the main national research and higher education cluster, member of the
Université Paris Saclay, a major actor in the French Investments for the Future Programme (Idex,
LabEx, IRT, Equipe) and partner of the main establishments present on the plateau, the centre is
particularly active in three major areas: data and knowledge; safety, security and reliability; modelling,
simulation and optimisation (with priority given to energy).

The 450 researchers and engineers from Inria and its partners who work in the research centre’s 31
teams, the 100 research support staff members, the high-level equipment at their disposal (image
walls, high-performance computing clusters, sensor networks), and the privileged relationships with
prestigious industrial partners, all make Inria Saclay Île-de-France a key research centre in the local
landscape and one that is oriented towards Europe and the world.

Context
This thesis subject is offered at Inria Saclay IdF (https://www.inria.fr/en/centre/saclay) in the
LIFEWARE project-team (http://lifeware.inria.fr), in the framework of the ANR-DFG SYMBIONT project
on “Symbolic Methods for Biological Networks” (https://www.symbiont-project.org).

The LIFEWARE team works in computational systems biology and develops the Biochemical Abstract
Machine (BIOCHAM http://lifeware.inria.fr/biocham4) software for modeling, analyzing and now
synthesizing biochemical reaction networks (CRNs) using methods from fundamental computer
science and mathematics. The software developments are expected to be integrated in BIOCHAM.

The thesis will be supervised by François Fages who has supervised 29 Ph.D. theses in his career, the
last defended in May 2016, and who currently is 100% available with no Ph.D. student.

Assignment
Model reduction is a central topic in differential dynamical systems theory, for reducing the
complexity of differential equations, finding important parameters, and developing multi-scale
models for instance. While perturbation theory is a standard mathematical tool to analyze the
different time scales of a dynamical system, and decompose the system according to fast-slow
dynamics, in the domain of computational systems biology, the biochemical reaction networks under
consideration involve several tenths of variables which appeal for automated reasoning methods.

Tropicalization is a mathematical method for analysing polynomial equations in the (min,+)
(full addition and min) semiring. The intuitive idea is to reason on the orders of magnitude of concentrations and
kinetic parameters which are expressed by the logarithm of their values, hence the (min,+)
semiring. We have shown that Constraint Logic Programming can be used to efficiently solve
tropical equation problems for identifying the dominating monomials and reactions in a network, and
then simplifying the dynamics in the different regions of the phase space corresponding to different
regimes (i.e. Quasi Steady State or Quasi Equilibrium assumptions).

The goal of this Thesis, in collaboration with our partners of the ANR-DFG project SYMBIONT, is to
generalize our tropical equation solver based on constraint programming to new stability constraints,
and to develop the model reduction method by searching for precise approximation results (e.g. using
Tikhonov theorem) at least in simple examples like the Michaelis-Menten enzymatic reaction. The
method will be implemented in our modeling environment Biocham, evaluated on mcell systems
biology models from BioModels repository, and compared to other symbolic methods developed in
SYMBIONT.

Main activities
Our first results on this subject have been published in

Sylvain Soliman, François Fages, Ovidiu Radulescu. A constraint solving approach to model reduction

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be submitted online on the Inria
The planned work will consist in:

- generalizing the CLP solver to handle inequalities instead of equalities, with accurate translation from polynomials to \((\min,+)\) intervals,
- developing correctness criteria for the simplified system (e.g. stability conditions of Tikhonov theorem),
- implementing the model reduction method and evaluating it on models from the BioModels repository.

Further reading:


Skills

This subject requires common and basic knowledge on differential equations, linear algebra, algorithms and programming.

There is no specific prerequisite for this internship. However, some specific knowledge on either the algebra \((\max,+)\), constraint programming, control theory, or computational systems biology will be a plus.

Benefits package

- Subsidised catering service
- Partially-reimbursed public transport
- Social security
- Paid leave
- Flexible working hours
- Sports facilities

Remuneration

Monthly gross salary: 1.982 euros (1st and 2nd year) - 2.085 euros (3rd year)